Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

Claim 1. (withdrawn) A substantially complete ribozyme library comprising a collection of adeno-associated virus (AAV), retroviral, or Eppstein-Barr virus (EBV) vectors, or a collection of retroviral vectors containing nucleic acids encoding hairpin ribozymes in expression cassettes wherein said collection of AAV, retroviral, or EBV vectors contains nucleic acids encoding on average about 90% or more of all possible hairpin ribozyme binding sequences having eight or more randomized nucleotides.

Claim 2. (withdrawn) The ribozyme library of claim 1, wherein said collection of vectors contains nucleic acids encoding about 95% or more of all possible hairpin ribozyme binding sequences.

Claim 3. (withdrawn) The ribozyme library of claim 1, wherein said collection of vectors contains nucleic acids encoding about 95% or more of all possible hairpin ribozyme binding sequences having 9 or more randomized nucleotides.

Claim 4. (withdrawn) The ribozyme library of claim 1, wherein said collection of vectors contains nucleic acids encoding about 95% or more of all possible hairpin ribozyme binding sequences having 12 randomized nucleotides.

Claim 5. (withdrawn) The ribozyme library of claim 1, wherein said nucleic acids are plasmids.

Claim 6. (withdrawn) The ribozyme library of claim 1, wherein said library contains no toxic ribozymes.

Claim 7. (withdrawn) The ribozyme library of claim 1, wherein said collection of vectors is a collection of AAV vectors.

Claim 8. (withdrawn) The ribozyme library of claim 7, wherein said nucleic acids comprise a pair of inverted terminal repeats (ITRs) of adeno-associated viral genome.

Claim 9. (withdrawn) The ribozyme library of claim 1, wherein said nucleic acids comprise a selectable marker.

Claim 10. (withdrawn) The ribozyme library of claim 9, wherein said selectable marker is selected from the group consisting of Neo^r, amd $Hygro^r$.

Claim 11. (withdrawn) The ribozyme library of claim 10 wherein said selectable marker is operably linked to an SV40 promoter.

Claim 12. (withdrawn) The ribozyme library of claim 1, wherein the ribozyme-encoding nucleic acid is operably linked to a tRNA promoter.

Claim 13. (withdrawn) The ribozyme library of claim 1, wherein the ribozyme-encoding nucleic acid is operably linked to a promoter selected from the group consisting of tRNAval, tRNAser, and PGK.

Claim 14. (withdrawn) A substantially complete ribozyme gene library comprising a collection of plasmids wherein members of said collection encode a retroviral, adeno-associated virus (AAV), or Epstein Barr virus (EBV) vector containing a ribozyme-encoding nucleic acid and said collection of plasmids encodes on average about 90% or more of all possible hairpin ribozyme binding sequences having eight or more randomized nucleotides.

Claim 15. (withdrawn) The ribozyme gene library of claim 14, wherein said collection of plasmids encodes on average about 95% or more of all possible hairpin ribozyme binding sequences.

Claim 16. (withdrawn) The ribozyme gene library of claim 14, wherein said collection of plasmids encodes on average about 95% or more of all possible hairpin ribozyme binding sequences having 9 or more randomized nucleotides.

Claim 17. (withdrawn) The ribozyme gene library of claim 14, wherein said library contains essentially no toxic ribozymes.

Claim 18. (withdrawn) The ribozyme gene library of claim 14, wherein members of said collection encode an AAV vector.

Claim 19. (withdrawn) The ribozyme gene library of claim 18, wherein said nucleic acids comprise a pair of inverted terminal repeats (ITRs) of adeno-associated viral genome.

Claim 20. (withdrawn) The ribozyme gene library of claim 14, wherein said plasmids contain a selectable marker.

Claim 21. (withdrawn) The ribozyme gene library of claim 20, wherein said selectable marker is selected from the group consisting of Neo^r, and $Hygro^r$.

Claim 22. (withdrawn) The ribozyme gene library of claim 14, wherein said selectable marker is operably linked to an SV40 promoter.

Claim 23. (withdrawn) The ribozyme gene library of claim 14, wherein the ribozyme-encoding nucleic acid is operably linked to a tRNA promoter.

Claim 24. (withdrawn) The ribozyme gene library of claim 14, wherein the ribozyme-encoding nucleic acid is operably linked to a promoter selected from the group consisting of tRNAval, tRNAser, and PGK.

Claim 25. (original) A method of selecting a ribozyme that specifically binds and cleaves a nucleic acid target, said method comprising:

i) transfecting a population of cells with a substantially complete hairpin ribozyme library comprising a collection of adeno-associated virus (AAV), retroviral, or

Epstein Barr virus (EBV) vectors containing nucleic acids encoding hairpin ribozymes in expression cassettes wherein said collection of AAV, retroviral, or EBV vectors contains nucleic acids encoding on average about 90%or more of all possible hairpin ribozyme binding sequences having eight or more randomized nucleotides;

ii) detecting a phenotypic difference between a transfected cell that expresses at least one hairpin ribozyme encoded by said library and a control cell lacking an active members of said ribozyme library, wherein said phenotypic difference is a consequence of cleavage of said target; and

iii) recovering a ribozyme associated with said phenotypic difference.

Claim 26. (original) The method of claim 25, wherein said transfecting produces a population of cells stably transfected with an expression cassette encoding a hairpin ribozyme.

Claim 27. (original) The method of claim 25, wherein said hairpin ribozyme is constitutively expressed.

Claim 28. (original) The method of claim 25, wherein said recovering comprises isolating a multiplicity of ribozymes to produce a targeted ribozyme library.

Claim 29. (original) The method of claim 25, further comprising

iv) transfecting a population of cells with said targeted ribozyme library;

v) detecting a phenotypic difference between a transfected cell that expresses at least one hairpin ribozyme encoded by said targeted ribozyme library and a control cell lacking an active member of said ribozyme library, wherein said phenotypic difference is a consequence of cleavage of said target; and

vi) recovering a ribozyme associated with said phenotypic difference.

Claim 30. (original) The method of claim 25, wherein said recovering comprises isolating and sequencing the binding site of said ribozyme.

Claim 31. (original) The method of claim 25, further comprising providing a probe that hybridizes to the nucleic acid specifically bound by said ribozyme.

Claim 32. (original) The method of claim 25, wherein said probe is labeled.

Claim 33. (original) The method of claim 25, wherein phenotypic difference is a difference in transcription or expression of a reporter gene or cDNA.

Claim 34. (original) The method of claim 25, wherein phenotypic difference is the ability of a cell to grow on soft agar.

Claim 35. (original) The method of claim 25, wherein phenotypic difference is the ability of a cell to differentiate.

Claim 36. (original) The method of claim 35, wherein said ability to differentiate is identified by the adherence of the cell to a surface in culture.

Claim 37. (original) The method of claim 25, wherein said phenotypic difference is resistance to a drug.

Claim 38. (original) The method of claim 37, wherein said drug is selected from the group consisting of cisplatin, doxirubicin, taxol, camptothecin, daunorubicin, and methotrexate.

Claim 39. (original) The method of claim 25, wherein said phenotypic difference is a change in the expression level of a reporter gene linked to a gene whose regulation it is desired to alter.

Claim 40. (original) The method of claim 25, wherein said collection of AAV, retroviral, or EBV vectors contains nucleic acids encoding on average about 95% or more of all possible hairpin ribozyme binding sequences.

Claim 41. (original) The method of claim 25, wherein said collection of AAV, retroviral, or EBV vectors contains nucleic acids encoding on average about 90% or more of all possible hairpin ribozyme binding sequences having 9 or more randomized nucleotides.

Claim 42. (original) The method of claim 25, wherein said nucleic acids are plasmids.

Claim 43. (original) The method of claim 25, wherein said library contains no toxic ribozymes.

Claim 44. (original) The method of claim 25, wherein said collection of vectors is a collection of AAV vectors.

Claim 45. (original) The method of claim 44, wherein said nucleic acids comprise a pair of inverted terminal repeats (ITRs) of adeno-associated viral genome.

Claim 46. (original) The method of claim 25, wherein said nucleic acids comprise a selectable marker.

Claim 47. (original) The method of claim 46, wherein said selectable marker is selected from the group consisting of Neo^r and $Hygro^r$.

Claim 48. (original) The method of claim 47, wherein said selectable marker is operably linked to an SV40 promoter.

Claim 49. (original) The method of claim 25, wherein the ribozyme-encoding nucleic acid is operably linked to a tRNA promoter.

Claim 50. (original) The method of claim 25, wherein the ribozyme-encoding nucleic acid is operably linked to a promoter selected from the group consisting of tRNAval, tRNAser, and PGK.

Claim 51. (withdrawn) A method of identifying a gene or mRNA altered expression of which results in alteration of a detectable phenotypic character, said method comprising:

i) stably transfecting a population of cells with a hairpin ribozyme library comprising a collection of adeno-associated virus (AAV) vectors containing nucleic acids encoding hairpin ribozymes in expression cassettes;

ii) detecting a phenotypic difference between a transfected cell that expresses said hairpin ribozyme and a control cell lacking an active form of said hairpin ribozyme;

iii) recovering a ribozyme associated with said phenotypic difference; and

iv) sequencing the binding site sequence of the recovered ribozyme to identify the nucleic acid to which it bound.

Claim 52. (withdrawn) The method of claim 51, wherein said hairpin ribozyme is constitutively expressed.

Claim 53. (withdrawn) The method of claim 51, wherein said ribozyme library is a substantially complete ribozyme library.

Claim 54. (withdrawn) The method of claim 51, wherein said ribozyme library is a targeted ribozyme library.

Claim 55. (withdrawn) The method of claim 51, wherein said recovering comprises reverse transcribing and amplifying the nucleic acid comprising said ribozyme..

Claim 56. (withdrawn) The method of claim 55, further comprising providing a probe that hybridizes to the nucleic acid specifically bound by said ribozyme.

Claim 57. (withdrawn) The method of claim 56, wherein said probe is labeled.

Claim 58. (withdrawn) The method of claim 51, wherein said phenotypic difference is a difference in transcription or expression of a reporter gene or cDNA.

Claim 59. (withdrawn) The method of claim 51, wherein said phenotypic difference is the ability of a cell to grow on soft agar.

Claim 60. (withdrawn) The method of claim 51, wherein said phenotypic difference is the ability of a cell to differentiate.

Claim 61. (withdrawn) The method of claim 60, wherein said ability to differentiate is identified by the adherence of the cell to a surface in culture.

Claim 62. (withdrawn) The method of claim 51, wherein phenotypic difference is resistance to a drug.

Claim 63. (withdrawn) The method of claim 62, wherein said drug is selected from the group consisting of cisplatin, doxirubicin, taxol, camptothecin, daunorubicin, and methotrexate.

Claim 64. (withdrawn) The method of claim 51, wherein said phenotypic difference is a change in the expression level of a reporter gene linked to a gene whose regulation it is desired to alter.

Claim 65. (original) A method of producing a cell line having altered expression of a gene said method comprising stably transfecting a cell with a vector encoding a hairpin ribozyme wherein said hairpin ribozyme is identified according to the method of claim 25.

Claim 66. (withdrawn) A population of mammalian cells containing a substantially complete ribozyme library comprising a collection of adeno-associated virus (AAV), retrovirus, or Epstein Barr virus (EBV) vectors containing nucleic acids encoding hairpin ribozymes in expression cassettes wherein said collection of AAV, retroviral, or EBV vectors contains nucleic acids encoding on average about 90% or more of all possible hairpin ribozyme binding sequences having eight or more randomized nucleotides.

Claim 67. (withdrawn) The ribozyme library of claim 66, wherein said collection of AAV, retroviral, or EBV vectors contains nucleic acids encoding about 95% or more of all possible hairpin ribozyme binding sequences.

Claim 68. (withdrawn) The ribozyme library of claim 66, wherein said collection of AAV, retroviral, or EBV vectors contains nucleic acids encoding about 95% or more of all possible hairpin ribozyme binding sequences having 9 or more randomized nucleotides.

Claim 69. (withdrawn) The ribozyme library of claim 66 wherein said collection of AAV, retroviral, or EBV vectors contains nucleic acids encoding about 95% or more of all possible hairpin ribozyme binding sequences having 12 randomized nucleotides.

Claim 70. (withdrawn) A kit comprising one or more containers containing

a substantially complete ribozyme library comprising a collection of adeno-associated virus (AAV), retrovirus, or Epstein Barr virus (EBV) vectors containing nucleic acids encoding hairpin ribozymes in expression cassettes wherein said collection of AAV, retroviral, or EBV vectors contains nucleic acids encoding on average about 90% or more of all possible hairpin ribozyme binding sequences having eight or more randomized nucleotides; or

a substantially complete ribozyme gene library comprising a collection of plasmids wherein members of said collection encode a retroviral, adeno-associated virus (AAV), or Epstein Barr virus (EBV) vector containing a ribozyme-encoding nucleic acid and said collection of plasmids encodes on average about 90% or more of all possible hairpin ribozyme binding sequences having eight or more randomized nucleotides.

Claim 71. (previously presented) A method for identification of a nucleic acid molecule that modulates a process in a biological system comprising the steps of:

a) introducing a random library of a nucleic acid catalyst into said biological system under conditions suitable for modulating said process, wherein said nucleic acid catalyst comprises a substrate binding domain and a catalytic domain, said substrate binding domain comprises a random sequence; and

b) determining the nucleotide sequence of at least a portion of the substrate binding domain of said nucleic acid catalyst from said biological system in which the process has been modulated.

Claim 72. (previously presented) A method for identifying one or more nucleic acid molecules involved in a process in a biological system comprising the steps of:

a) providing a library of a nucleic acid catalyst, with a substrate binding domain and a catalytic domain, wherein said substrate binding domain comprises a random sequence, to said biological system under conditions suitable for said process to be altered;

b) identifying any said nucleic acid catalyst present in said biological system where said process has been altered; and

c) determining the nucleotide sequence of at least a portion of the binding domain of said any said nucleic acid catalyst to allow said identification of said nucleic acid molecule involved in said process in said biological system.

Claim 73. (previously presented) A method for identification of a nucleic acid catalyst that modulates a process in a biological system comprising the steps of:

a) introducing a random library of a nucleic acid catalyst into said biological system under conditions suitable for modulating said process, wherein said nucleic acid catalyst comprises a substrate binding domain and a catalytic domain, said substrate binding domain comprises a random sequence; and

b) identifying said nucleic acid catalyst from said biological system in which the process has been modulated.

Claim 74. (previously presented) The method of any of claims 71-73, wherein said biological system is a bacterial cell.

Claim 75. (previously presented) The method of any of claims 71-73, wherein said biological system is of plant origin.

Claim 76. (previously presented) The method of any of claims 71-73, wherein said biological system is of mammalian origin.

Claim 77. (previously presented) The method of any of claims 71-73, wherein said nucleic acid catalyst is in a hammerhead motif.

Claim 78. (previously presented) The method of any of claims 71-73, wherein said nucleic acid catalyst is in a hairpin motif.

Claim 79. (previously presented) The method of any of claims 71-73, wherein said nucleic acid catalyst is in a group I intron ribozyme motif, group II intron ribozyme motif, VS ribozyme motif or RNase P ribozyme motif.

Claim 80. (previously presented) The method of any of claims 71-73, wherein said process is selected from the group consisting of growth, proliferation, apoptosis, morphology, angiogenesis, differentiation, migration, viral multiplication, drug resistance, signal transduction, cell cycle regulation, temperature sensitivity and chemical sensitivity.

Claim 81. (previously presented) The method of any of claims 71-73, wherein said random library of nucleic acid catalysts is encoded by an expression vector in a manner which allows expression of said nucleic acid catalysts.

Claim 82. (previously presented) The method of claim 81, wherein said expression vector comprises:

a) a transcription initiation region;

b) a transcription termination region;

c) a sequence encoding at least one said nucleic acid catalyst; and

wherein said sequence is operably linked to said initiation region and said termination region, in a manner which allows expression or delivery or expression and delivery of said nucleic acid catalyst.

Claim 83. (previously presented) The method of claim 81, wherein said expression vector comprises:

a) a transcription initiation region;

b) a transcription termination region;

c) an open reading frame for a polypeptide;

d) a sequence encoding at least one said nucleic acid catalyst,

wherein said sequence is operably linked to the 3'-end of said open reading frame; and wherein said sequence is operably linked to said initiation region, said open reading frame and said termination region, in a manner which allows expression or delivery or expression and delivery of said nucleic acid catalyst.

Claim 84. (previously presented) The method of claim 81, wherein said expression vector comprises:

a) a transcription initiation region;

b) a transcription termination region;

c) an intron;

d) a sequence encoding at least one said nucleic acid catalyst; and

wherein said sequence is operably linked to said initiation region, said intron and said termination region, in a manner which allows expression or delivery or expression and delivery of said nucleic acid catalyst.

Claim 85. (previously presented) The method of claim 81, wherein said expression vector comprises:

a) a transcription initiation region;

b) a transcription termination region;

c) an intron;

d) an open reading frame for a polypeptide;

e) a sequence encoding at least one said nucleic acid catalyst,

wherein said sequence is operably linked to the 3'-end of said open reading frame; and

wherein said sequence is operably linked to said initiation region, said intron, said open reading frame and said termination region, in a manner which allows expression or delivery or expression and delivery of said nucleic acid catalyst.

Claim 86. (previously presented) The method of claim 81, wherein said expression vector is derived from a retrovirus.

Claim 87. (previously presented) The method of claim 81, wherein said expression vector is derived from an adenovirus.

Claim 88. (previously presented) The method of claim 81, wherein said expression vector is derived from an adeno-associated virus.

Claim 89. (previously presented) The method of claim 81, wherein said expression vector is derived from an alphavirus.

Claim 90. (previously presented) The method of claim 81, wherein said expression vector is derived from a bacterial plasmid.

Claim 91. (previously presented) The method of claim 81, wherein said expression vector is operably linked to a RNA polymerase II promoter element.

Claim 92. (previously presented) The method of claim 81, wherein said expression vector is operably linked to a RNA polymerase III promoter element.

Claim 93. (previously presented) The method of claim 92, wherein said RNA polymerase III promoter is derived from a transfer RNA gene.

Claim 94. (previously presented) The method of any of claims 71-73, wherein said biological system is of an eukaryotic origin.

Claim 95. (previously presented) The method of any of claims 71-73, wherein said biological system is of an prokaryotic origin.

Claim 96. (previously presented) The method of any of claims 71-73, wherein said substrate binding domain is of length between 12 and 100 nucleotides.

Claim 97. (previously presented) The method of any of claims 71-73, wherein said substrate binding domain is of length between 14 and 24 nucleotides.

Claim 98. (previously presented) The method of any of claims 71-73, wherein said nucleic acid catalyst comprises two substrate binding arms.

Claim 99. (previously presented) The method of claim 98, wherein said substrate binding arms are of similar length.

Claim 100. (previously presented) The method of claim 98, wherein said substrate binding arms are of different length.

Claim 101. (new) A method for identifying a gene that modulates a process in a biological system comprising the steps of:

a) introducing a library of nucleic acid catalysts into a biological system under conditions suitable for modulating a process in the biological system, wherein each nucleic acid catalyst comprises a substrate binding domain and a catalytic domain and the substrate binding domain comprises a random sequence;

b) determining the nucleotide sequence of at least a portion of the substrate binding domain of any nucleic acid catalyst in the biological system in which the process has been modulated; and

c) identifying a gene that modulates a process in a biological system using the nucleotide sequence from step (b).

Claim 102. (new) A method for identifying a gene involved in a biological process comprising the steps of:

a) introducing a library of nucleic acid catalysts into a biological system under conditions suitable for altering a process in the biological system, wherein each nucleic acid catalyst comprises a substrate binding domain and a catalytic domain and the substrate binding domain comprises a random sequence;

b) identifying any nucleic acid catalyst in the biological system in which the biological process has been altered; and

c) determining the nucleotide sequence of at least a portion of the substrate binding domain of any nucleic acid catalyst from step (b) to identify a gene involved in said biological process.

Claim 103. (new) A method comprising the steps of:

a) providing a random binding arm nucleic acid catalyst library to a biological system under conditions suitable for a nucleic acid catalyst from the library to down-regulate the expression of a gene;

b) determining the biological system in which the expression of a gene has been down-regulated;

c) determining the nucleotide sequence of at least one portion of the binding arm of the nucleic acid catalyst in the biological system of step (b); and

d) identifying the gene which expression is down-regulated using the nucleotide sequence from step (c).

Claim 104. (new) The method of any of claims 101-103, wherein said nucleic acid catalyst is in a group I intron ribozyme motif, group II intron ribozyme motif hepatitis delta virus ribozyme motif, VS ribozyme motif or RNase P ribozyme motif.

Claim 105. (new) The method of any of claims 101-103, wherein said nucleic acid catalyst is in a hammerhead ribozyme motif.

Claim 106. (new) The method of any of claims 101-103, wherein said nucleic acid catalyst is in a hairpin ribozyme motif.

Claim 107. (new) The method of any of claims 101-103, wherein said biological system is a bacterial cell.

Claim 108. (new) The method of any of claims 101-103, wherein said biological system is of plant origin.

Claim 109. (new) The method of any of claims 101-103, wherein said biological system is of mammalian origin.

Claim 110. (new) The method of claim 100 or claim102, wherein said process is selected from the group consisting of growth, proliferation, apoptosis, morphology, angiogenesis, differentiation, migration, viral multiplication, drug resistance, signal transduction, cell cycle regulation, temperature sensitivity and chemical sensitivity.

Claim 111. (new) The method of any of claims 101-103, wherein said library of nucleic acid catalysts is encoded by an expression vector in a manner which allows expression of said nucleic acid catalysts.

Claim 112. (new) The method of claim 111, wherein said expression vector comprises:

a) a transcription initiation region;

b) a transcription termination region; and

c) a sequence encoding at least one said nucleic acid catalyst,

wherein said sequence is operably linked to said initiation region and said termination region, in a manner which allows expression or delivery or expression and delivery of said nucleic acid catalyst.

Claim 113. (new) The method of claim 111, wherein said expression vector comprises:

a) a transcription initiation region;

b) a transcription termination region;

c) an open reading frame for a polypeptide; and

d) a sequence encoding at least one said nucleic acid catalyst,

wherein said sequence is operably linked to the 3'-end of said open reading frame; wherein said sequence is operably linked to said initiation region, said open reading frame and said termination region, in a manner which allows expression or delivery or expression and delivery of said nucleic acid catalyst.

Claim 114. (new) The method of claim 111, wherein said expression vector comprises:

a) a transcription initiation region;

b) a transcription termination region;

c) an intron; and

d) a sequence encoding at least one said nucleic acid catalyst,

wherein said sequence is operably linked to said initiation region, said intron and said termination region, in a manner which allows expression or delivery or expression and delivery of said nucleic acid catalyst.

Claim 115. (new) The method of claim 111, wherein said expression vector comprises:

a) a transcription initiation region;

b) a transcription termination region;

c) an intron;

d) an open reading frame for a polypeptide; and

e) a sequence encoding at least one said nucleic acid catalyst,

wherein said sequence is operably linked to the 3'-end of said open reading frame; wherein said sequence is operably linked to said initiation region, said intron, said open reading frame and

said termination region, in a manner which allows expression or delivery or expression and delivery of said nucleic acid catalyst.

Claim 116. (new) The method of claim 111, wherein said expression vector is derived from a retrovirus.

Claim 117. (new) The method of claim 111, wherein said expression vector is derived from an adenovirus.

Claim 118. (new) The method of claim 111, wherein said expression vector is derived from an adeno-associated virus.

Claim 119. (new) The method of claim 111, wherein said expression vector is derived from an alphavirus.

Claim 120. (new) The method of claim 111, wherein said expression vector is derived from a bacterial plasmid.

Claim 121. (new) The method of claim 111, wherein said expression vector is operably linked to a RNA polymerase II promoter element.

Claim 122. (new) The method of claim 111, wherein said expression vector is operably linked to a RNA polymerase III promoter element.

Claim 123. (new) The method of claim 122, wherein said RNA polymerase III promoter is derived from a transfer RNA gene.

Claim 124. (new) The method of any of claims 101-103, wherein said biological system is of an eukaryotic origin.

Claim 125. (new) The method of any of claims 101-103, wherein said biological system is of an prokaryotic origin.

Claim 126. (new) The method of any of claims 101-103, wherein said substrate binding domain is of a length between 12 and 100 nucleotides.

Claim 127. (new) The method any of claims 101-103, wherein said substrate binding domain is of a length between 14 and 24 nucleotides.

Claim 128. (new) The method of any of claims 101-103, wherein said substrate binding domain comprises two substrate binding arms.

Claim 129. (new) The method of claim 128, wherein said substrate binding arms are of similar length.

Claim 130. (new) The method of claim 128, wherein said substrate binding arms are of different length.